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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,579	05/15/2002	Bernt Sweder Van Asbeck	30394-1064	7721

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EXAMINER	
STUCKER, JEFFREY J	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 01/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Acti n	Application No.	Applicant(s)	
	10/049,579	VAN ASBECK ET AL.	
	Examiner	Art Unit	
	Jeffrey Stucker	1648	

--The MAILING DATE of this communication appears on the cover sh et with the correspondence address --

THE REPLY FILED 16 December 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See attached Advisory Action*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1 and 3-27*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☒ Note the attached Information Disclosure Statement(s)(PTO-1449) ~~Paper No(s)~~ filed. *16 December 2004*.

10. ☐ Other: _____

This Office Action is in response to the amendment filed 16 December 2004. Claims 1 and 3-27 are pending and remain under final rejection.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

The correction to the claim numbering is noted and is entered because it simplifies the issues for appeal.

The rejection of claims 1, 5, 7-9, and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Ohta et al. (Biological & pharmaceutical Bulletin, Feb. 1999) is maintained.

Applicant's arguments have been fully considered but are not deemed to be persuasive. Applicant argues the synergistic effect of KM043 and bleomycin shown for cancer cells is not taught to hold for the inhibition of virus replication; bleomycin would worsen a patient's immune system; and Van Asbeck et al. showed that bleomycin at concentration which inhibited viral replication had no influence on the viability of HIV infected cells; and that the anti-cancer effect of bleomycin is not the same, and does not anticipate the used of bleomycin as a virus killer.

This is not convincing because it is not relevant whether there is a synergistic effect in treating virus; the reference teaches that HIV RT is inhibited. That the treatment my worsen a patient's immune system is not well taken as bleomycin, a commonly used drug, does not worsen the immune system to the point that the drug is not used for cancer treatments. Thus, not only is the composition taught, but the reference clearly teaches that it inhibits HIV RT, so it therefore, has treated a viral infection, even if *in vitro*. Therefore, a composition comprising bleomycin and a reverse transcriptase inhibitor and method of treating HIV infection are anticipated by Ohta et al.

The rejection of claims 1, 3, 4, 7-11 are rejected under 35 U.S.C. 103(a) as obvious over Gompels et al. (AIDS, 1992) in view of Sham et al. (WO 97/21683) is maintained.

Applicant's arguments have been fully considered but are not deemed to be persuasive. Applicant argues that Gompels et al. does not affect HIV replication or describe treatment of HIV infection. Applicant argues that Sham et al. teaches HIV treatments but only protease inhibitors and posits that it would not be obvious to combine non-protease inhibitors with protease inhibitors. Applicant further argues that Gompels et al. teaches bleomycin to treat Kaposi's, and zidovudine, a known

anti-HIV drug, to treat HIV. Applicant also argues that bleomycin is toxic and it would not be obvious to reduce the dosage.

This is not convincing because, as applicant notes, Kaposi's is not caused by HIV infection, but is a common sequela to HIV/AIDS. It would be readily apparent to the artisan to treat both the symptom of the disease (Kaposi's) and the root cause (HIV infection) in order to eliminate the immediate cancer threat and the long term HIV threat. Applicant's arguments about the lack of reason as to use a second drug with the same target in order to reduce toxicity is not convincing because bleomycin and zidovudine have different targets, and as Applicant recognizes, Gompels et al. teaches that both bleomycin and zidovudine can be used to treat disease. Applicant has not addressed why it would not be obvious for the ordinary artisan to substitute one known anti-HIV drug for another, as set forth in the previous Office Action. Thus, the instant invention is obvious over Gompels et al. in view of Sham et al.

The rejection of claims 1, 5-9, 12, and 13 are rejected under 35 U.S.C. 103(a) as obvious over Gompels et al. (AIDS, 1992) in view of Malley et al. is maintained.

Applicant's observation concerning the rejection of the claims in view of Malley et al. is correct. The Examiner apologizes for the oversight and any confusion caused by it.

Applicant's arguments have been fully considered but are not deemed to be persuasive. Applicant argues that because Malley et al. teaches combination therapy using dideoxyinosine and hydroxamate derivatives, it would not be obvious to combine bleomycin with dideoxyinosine.

This is not convincing because applicant is arguing the references separately. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Thus, the instant invention is obvious over Gompels et al. in view of Malley et al.

The rejection of claims 14-17 and 20-25 are rejected under 35 U.S.C. 103(a) as obvious over Andrus et al. (Biochemical pharmacology, 1998) in view of Sham et al. (WO 97/21683) is maintained.

Applicant's arguments have been fully considered but are not deemed to be persuasive. Applicant argues that the deferiprone of Andrus et al. is different from the deferiprone of the instant invention and that the way it is used is not the same. Applicant further argues that Sham et al. does not speak about a more effective treatment or a stronger or synergistic effect as a reason for combining substances and that the reference does not teach that combination therapy is more efficient or obvious, and that the instant invention is aimed at a synergistic effect. Applicant further argues that the combination of deferiprone with another compound is never mentioned or suggested in the literature, that non-obviousness of combination therapy in view of Sham et al. appear from the fact that Sham et al. claims combination therapy for its own new compounds and that is not obvious to claim a combination of compounds as a combination can also result in the absence of beneficial effects or even adverse effects thus requiring investigation into possible combinations for an advantageous effect.

Applicant's arguments are not convincing because, as an initial matter, the deferiprone of Andrus et al. and the deferiprone of the instant invention are exactly alike. Whether Sham et al. speaks about a more effective treatment or a

stronger or synergistic effect as a reason for combining substances and that the reference does not teach combination therapy is more efficient or obvious is not relevant to the fact that the reference teaches multiple compounds for treatment. A synergistic effect is not required for combining, merely that there be an expected benefit. It is not clear how or why one would expect the absence of beneficial effects or the occurrence of adverse effects when the compounds are known to be beneficial. The motivation to combine the references of Andrus et al. with Sham et al. has been discussed in the Final Office Action. Thus, the instant invention is obvious over Andrus et al. in view of Sham et al.

The rejection of claims 14, 15, 18-23, 26, and 27 are rejected under 35 U.S.C. 103(a) as obvious over Andrus et al. (Biochemical pharmacology, 1998) in view of Malley et al. (PNAS, 1994) is maintained.

Applicant's arguments have been fully considered but are not deemed to be persuasive. Applicant argues that it would not be obvious to combine an iron chelating compound with another compound such as an RT inhibitor as is instantly claimed because Gompels et al. teach bleomycin to treat Kaposi's and Zidovudine, a known anti-HIV drug to treat HIV.

This is not convincing because Applicant has not explained why it would not be obvious for the ordinary artisan to substitute one known anti-HIV drug for another, as set forth in the previous Office Action, with a reasonable expectation of success at treating both Kaposi's and HIV infection. Thus, the instant invention is obvious over Andrus et al. in view of Malley et al.

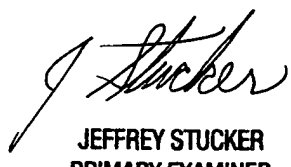
No claims are allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Stucker whose telephone number is (571)-272-0911. The examiner can normally be reached Monday to Thursday from 7:00am-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (571)-272-0902.



JEFFREY STUCKER
PRIMARY EXAMINER